REMARKS

These papers are submitted in response to the Office Action dated December 11, 2006. Applicants request entry of the Amendment and Response and reconsideration of the rejection of the claims in view of the following remarks. This Response is submitted within the two-month due date therefore, an Advisory Action is requested.

With entry of this amendment, Claims 16 is amended to specify that the immediate release second portion includes stabilized misoprostol. Claim 21 is canceled. Claims 22 and 23 are amended editorially and to change dependency due to cancellation of claim 21 and amendment of claim 16. Claims 19, 20, and 25 are amended to correct spelling errors. Claims 27, 28, and 29 are amended to provide clear antecedent basis and correct spelling errors. New claims 30-35 are added, with support found in previous claims 18-29, and throughout the specification, including for example, at paragraph [0033]-[0038], and [0046]-[0052] (page 6, line 18 to page 7, line 30; and page 9, line 5 and page 10, line 23).

35 USC § 112

Claims 27-29 stand rejected for reciting "The method to claim 20..." The claims are amended to correct the reference to claim 20.

35 USC § 103

Claims 16 and 18-29 are rejected as allegedly being obvious over Woolfe et al., US 2002/0054908 in view of Ouali, US 2003/0138486.

To support a rejection under 35 U.S.C. section 103, the collective teachings of the prior art must have suggested to one of ordinary skill in the art that, at the time the invention was made, applicant's claimed invention would have been obvious. In particular, a prima facie case of obviousness requires the references when combined must teach or suggest all of the claim limitations. Applicants submit that all of these requirements have not been met.

Independent claim 16, as amended is directed to an extended-release first portion of NSAIDs and an immediate release second portion made of stabilized misoprostol, wherein the extended release first portion and the immediate release second portion are encapsulated within a capsule made of hydroxyl-propyl-methyl-cellulose (HPMC) polymer.

In contrast the cited references, --Gimet, --Woolfe, or --Chemburkar or Sherman in view of Ouali do not teach extended release formulations, in particular compounding an NSAID with one or more retardants for extended release. Gimet, Woolfe, Chemburkar, Sherman and Ouali all rely on enteric coatings, which is a form of delayed release. The enteric coating on the cores or granules of the references delays absorption, targeting release in the intestine rather than the stomach. Once the enteric coating is penetrated, the cores and granules are rapidly disintegrated.

In contrast, the claimed pharmaceutical compositions require a dual-release solid pharmaceutical composition wherein an extended-release first region comprising at least one NSAID and a retardant material, is combined with an immediate release second region comprising a stabilized gastroprotective prostaglandin –both portions encapsulated within an HPMC capsule. As argued above, the cited references do not teach compounding retardant materials with an NSAID for form an extended-release portion, and further do not propose combining an extended-release NSAID with an immediate release prostaglandin. Furthermore, the nature of extended-release is sufficiently different from simple delayed release and enteric coated NSAIDS. The extended-release NSAID with retardant as claimed is released gradually throughout the gastrointestinal system starting from an oral administration in order to obtain release of the NSAID in the stomach and the intestine. In contrast, delayed release formulations (.e.g, enteric coatings) are used with the purpose of isolating complete release of the encapsulated compound to the small intestines for the purpose of avoiding NSAID contact with the stomach and possible stomach problems. Therefore, the teachings of the cited references for use of delayed release, including enteric coatings is not sufficient to reach the claimed pharmaceutical composition.

In addition, use of a gelatin capsule instead of an HPMC capsule are not acceptable equivalents for use in encapsulating the claimed two portion pharmaceutical composition. In particular, it has been found that an unexpected increase in stability of the pharmaceutical composition in the HPMC capsules. Applicants present a Declaration under 37 C.F.R. § 1.132 by Dr. Michel Franz providing evidence of the discovery that HPMC capsules provide a clear advantage over gelatin capsules.

The Applicants respectfully disagree with the Office's assertion that the provided Declaration does not present a side-by-side comparison. The claims, as amended, are limited to

misoprostol, which is the prostaglandin tested. Second, the Declaration compares HPMC capsules containing extended release Diclofenac Sodium pellets and one immediate release Misoprostol mini-tablet with gelatin capsules containing the same materials over a period of 6 months. This is a most valuable comparison for considering the enhanced results of the HPMC capsules versus gelatin capsules since the only change between the compared products is the capsule material.

A second Declaration by an independent expert, Dr. Karim Amighi from the Free University of Brussels, is provided. Dr. Karim Amighi indicates that extended-release NSAIDS (e.g., present application) and delayed-release NSAIDS (e.g., Wolfe) are known to be stable. Consequently, it is concluded that changing the extended-release Diclofenac Sodium pellets of the present invention for a delayed-release form of Diclofenac, such as is described by Wolfe, would not affect the surprising results that use of HPMC capsules for carrying an immediate release misoprostol in combination with an NSAID provide improved results over use of gelatin capsules.

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,
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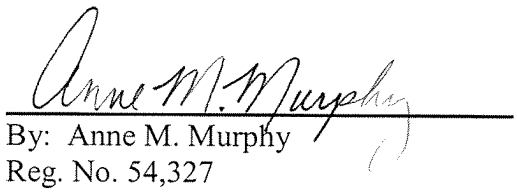
Date: February 12, 2007



By: Anne M. Murphy
Reg. No. 54,327

Attachments:
Declaration of Dr. Michel Franz w/ Exhibitions A & B
Declaration of Dr. Karim Amighi